

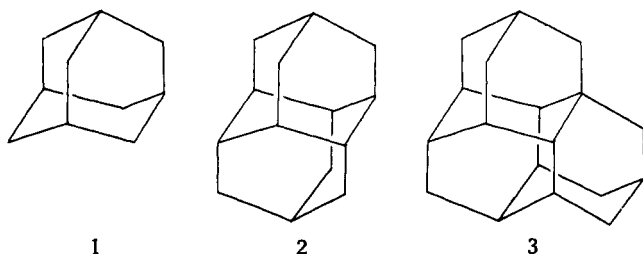
A New Approach to the Construction of Diamondoid Hydrocarbons. Synthesis of *anti*-Tetramantane

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Abstract: A new approach to the construction of diamondoid hydrocarbons is described. The method is general and could, in principle, be used as either a single or a double homologation of any lower member of the diamondoid series into a higher member. It is illustrated by the conversion of diamantane into triamantane (single homologation) and by the first synthesis of *anti*-tetramantane (double homologation), one of three topological forms of the fourth member of the diamondoid series. The sequence uses a keto-carbenoid insertion reaction to attach one or two cyclopentane rings to the diamantane periphery and terminates in an unusual gas-phase rearrangement-cyclization reaction on a platinum-silica catalyst. Some physical and spectral properties of *anti*-tetramantane are discussed.

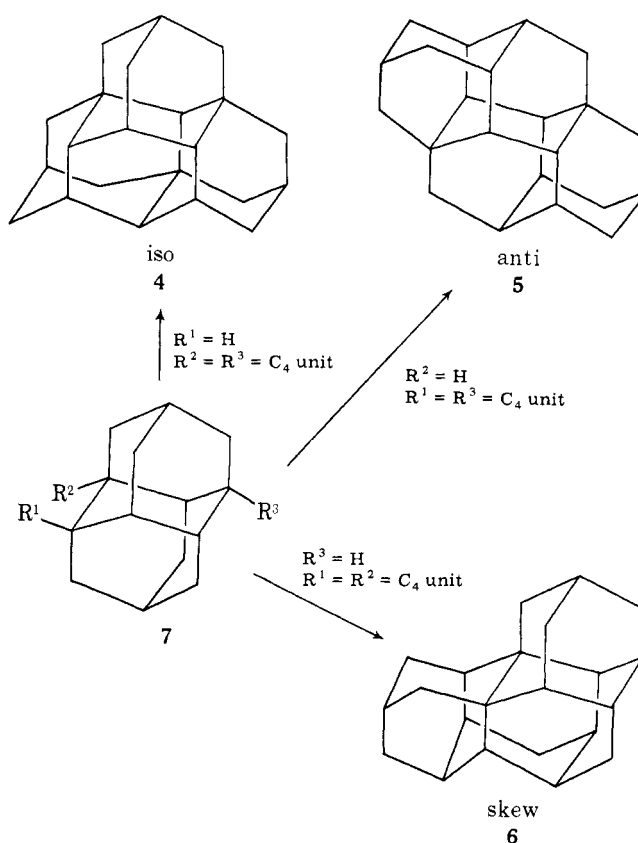
The diamondoid hydrocarbons constitute an homologous series of polycyclic structures, $C_{4n+6}H_{4n+12}$, whose topography is based on the regular repetitious array of tetrahedral carbon atoms found in diamond. Adamantane (1),^{2a} diamantane (2),^{2b} (formerly called congreane), and triamantane³ (3), the first



three members of the series, have been known for some time. Adamantane and diamantane are in fact naturally occurring substances, having been isolated from the crude petroleum oil of Hodonin in Czechoslovakia.^{2a,4} We now describe the first synthesis of tetramantane using a route which may be generally applicable to higher members of the series.

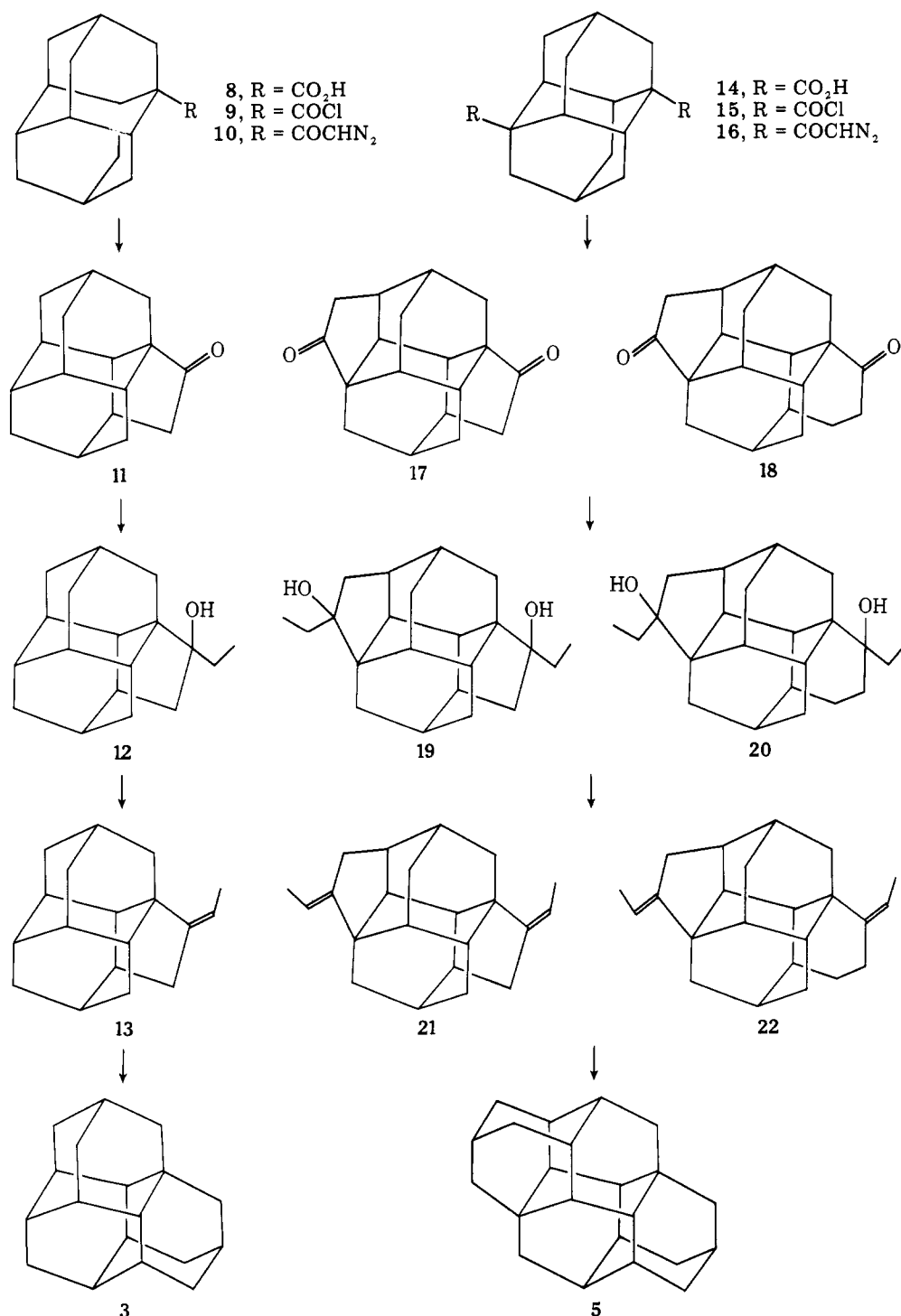
The lower diamondoid hydrocarbons are best synthesized by the so-called thermodynamic rearrangement route⁵ whose success rests on a number of factors: first, the high thermodynamic stability of each member of the diamondoid series relative to that of isomeric hydrocarbons, e.g., the energy change in the conversion of perhydrodicyclopentadiene into adamantane is about 16 kcal/mol exothermic;⁶ second, the availability of suitable precursors which, ideally, should be isomeric with the desired product; and third, the ability of certain Lewis acids to produce and sustain the cationic intermediates essential to the propagation of the rearrangement and the establishment of equilibrium.⁷

There are limitations, however, not the least of which is the problem of finding suitable precursors. This is no longer a problem with adamantane,⁵ diamantane,^{8,9} and triamantane,¹⁰ for which excellent, readily accessible precursors have now been found. It does become a problem in attempting to extend the series beyond triamantane since few large (≥ 22 carbon atoms) polycyclic hydrocarbons of molecular formula $C_{4n+6}H_{4n+12}$ are known. There is an additional complication, however, which only becomes apparent with the fourth member of the series, tetramantane, but which becomes a dominant feature of synthetic approaches to the higher members. Just as the familiar aliphatic hydrocarbon series branches at butane, so does the diamondoid series at tetramantane, giving rise to three possible forms designated¹¹ isotetramantane, C_{3v} (4), *anti*-tetramantane, C_{2h} (5), and *skew*-tetramantane, C_2 (6),¹² to emphasize their close topological relationship to isobutane



and the *anti* and *skew* conformations of *n*-butane, respectively. Accordingly, the possibility of producing complex mixtures of isomers may become a limiting factor in the Lewis acid rearrangement route. Finding a precursor of the correct molecular formula does not guarantee success even though the rearrangement may appear very feasible thermodynamically. In attempting to synthesize one or other of the tetramantane isomers Schleyer and his co-workers¹¹ prepared a strained $C_{22}H_{28}$ polycycle from cyclooctatetraene only to find that this precursor did not rearrange fully into the diamondoid form but stopped short at a less regular structure. The failure of this attempt was ascribed to mechanistic difficulties, not thermodynamic.

We have devised a new approach to this problem of some generality.¹³ It is free of some of the uncertainties of the Lewis acid rearrangement approach and is based on the idea that it should be possible to elaborate one member of the diamondoid series into the next higher member by adding two new rings



with four carbon atoms (single homologation)¹⁴ or into the second higher member by adding four new rings utilizing eight carbon atoms (double homologation). The details of this approach were explored for the elaboration of diamantane into triamantane and then were applied to the first synthesis of a tetramantane isomer.

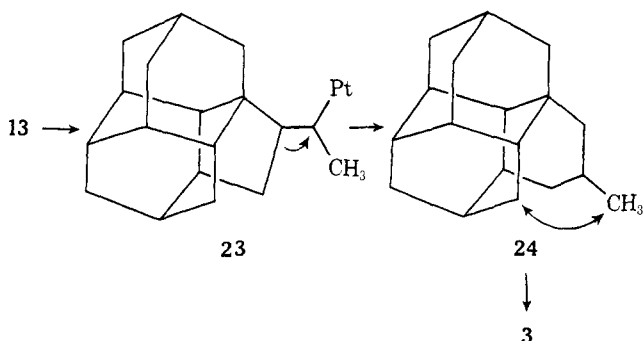
A four-carbon unit was added to the diamantane periphery via the carboxylic acid (**8**)¹⁵ with the first point of attachment at the 1 position. The acid was obtained by Koch-Haaf carboxylation of 1-diamantanol and was readily transformed into the acid chloride (**9**) with oxaloyl chloride in benzene at 20 °C. The action of ethereal diazomethane on the acid chloride produced the diazo ketone (**10**). The second point of attachment of the side chain was established by CuSO₄-catalyzed decomposition of the diazo ketone in hot toluene which led to

the crystalline cyclopentanone (**11**) in 47% yield.¹⁶ The remaining two carbon atoms were added via a Grignard reaction of the ketone with ethylmagnesium bromide and the mixture of epimeric tertiary alcohols (**12**) so produced was dehydrated in hot benzene containing iodine, furnishing the ethylidene hydrocarbon (**13**) of undetermined geometry about the double bond.

The final transformation was brought about on a platinum surface in the gas phase in hydrogen. The catalyst was prepared by impregnating silica gel with chloroplatinic acid sufficient to give a composition of 2% w/w in platinum. Water was removed by evaporation and the catalyst was reduced to the metallic state with a stream of hydrogen at 500 °C. When olefin **16** was vaporized in a stream of hydrogen and passed over the catalyst at 430 °C a mixture of products was obtained,

GLC analysis of which revealed the presence of one major and several minor components. Crystallization of the mixture from acetone gave triamantane in 21% yield.

Certain features of the mechanism of the final operation upon which this synthesis depends are worthy of comment. The overall change in **16**, involving expansion of the five-membered ring and carbon-carbon bond formation between the methyl group and a transannular methylene group, is reminiscent of and was planned on the chemistry of a well-known petrochemical process used in the production of benzene and alkylbenzenes from *n*-alkanes.¹⁷ *n*-Hexane, for example, is converted in the gas phase on platinum into methylcyclopentane and cyclohexane with subsequent dehydrogenation of the latter to benzene; furthermore, the ring expansion of methylcyclopentane to cyclohexane is also observed under the same conditions.^{18,19} Although the precise details are unknown, we envisage the formation of triamantane as proceeding via a surface alkyl such as **23** in which ring expansion occurs to the



carbon atom bonded to platinum,²⁰ producing the intermediate **24**. A second platinum-mediated reaction removes two hydrogen atoms from **24** with concomitant formation of a new carbon-carbon single bond. Control of the catalyst temperature was important. The optimum temperature for triamantane formation was 430 °C, combining a good conversion with minimum by-product formation and an acceptable weight recovery (70%). Temperatures of 20 °C or more above the optimum resulted in a subsequent reduction in the yield of triamantane, an increase in by-product formation, and a much reduced weight recovery. Below about 400 °C conversion to triamantane was low.

In turning to the more complex problem of double homologation of diamantane we were able to differentiate right at the outset between the structural foundations necessary for each of the three tetramantane isomers. Considering the relationship between the three possibilities and the precursor (**7**) it is clear that isotetramantane requires four carbon units at positions R_2 and R_3 , *anti*-tetramantane at positions R_1 and R_3 , and *skew*-tetramantane at R_1 and R_3 . Our efforts were directed toward the *anti* isomer. Prolonged exposure of diamantane to hot bromine produced a mixture of dibromides from which the 1,6 isomer²¹ could be obtained by fractional crystallization. The dibromide was hydrolyzed to the diol²² which on Koch-Haaf carboxylation furnished the 1,6-diacid **14** in excellent yield. Successive treatment of the diacid with oxaloyl chloride in boiling benzene and ethereal diazomethane produced the crystalline bisdiaz ketone **16** in good yield. CuSO_4 -catalyzed decomposition of **16** in hot toluene yielded, after purification by chromatography, 15% of a substance which by all accounts was the sought-after biscyclopentanone. A slight ambiguity arises here in that the product has two possible forms, *syn* (**17**) and *anti* (**18**), and from the nature of the reaction we expected both to be formed. Efforts to show that both isomers were present were unsuccessful; nevertheless, we assumed that the product was an inseparable mixture of the two. Fortunately, one or other of the isomers was acceptable for our purposes. Prolonged treatment of the diketones with

ethereal ethylmagnesium bromide produced diols **19** and **20** which were dehydrated in benzene containing iodine, yielding dienes **21** and **22**, presumed to be a mixture of isomers. When the diene mixture was subjected to the rearrangement procedure on platinum in the gas phase at 350–360 °C a product consisting of several components was obtained. Three crystallizations from acetone yielded a single substance (10%), mp 173.5–174 °C, with a premelting transition at 159 °C, identified by x-ray diffraction as *anti*-tetramantane (**5**); full details of the x-ray analysis will be published elsewhere.²³

The yield of *anti*-tetramantane was sensitive to variations in the temperature of the catalyst bed. The optimum working temperature was about 350 °C, although weight recovery was only fair (40%). At temperatures above 360 °C the weight recovery was only 25%. At 400 °C the major product, in a greatly depleted weight yield, was in fact triamantane, resulting from complete scission of one four-carbon unit. A variety of catalyst modifications were examined. Changing the dispersion of platinum on silica to 0.2 or 5.0% had little or no effect. Introduction of alumina (10%) into the silica support of a 1.5% platinum catalyst adversely affected the yield of *anti*-tetramantane and substantially increased the amount of side products. A catalyst consisting of 0.2% tin²⁴ and 1.3% platinum on silica behaved exactly as did platinum alone. Changing the support from silica to pumice with 1.5% platinum decreased the yield of *anti*-tetramantane. Of the variations examined, 1.5% platinum on silica at 350–360 °C produced the best results.

anti-Tetramantane possesses a range of interesting physical and spectral properties. The melting point conforms to the trend toward lower melting point exhibited by the earlier members of the series; furthermore, in each case the melting point is preceded by an endothermic transition, two in the case of diamantane, to an orientationally disordered phase (mp and transition temperature in °C): adamantane (269, –65), diamantane (251, 174, 142), triamantane (224, 155), and *anti*-tetramantane (174, 159). The mass spectrum of *anti*-tetramantane is very similar to that of triamantane,³ both showing even less fragmentation than do adamantane and diamantane.²⁵ The parent ion of **5** (M^+ m/e 292) is by far the most intense; of the remainder only those at m/e 291 and 91 are of noticeable intensity, 30 and 13%, respectively. This type of behavior is consistent with a highly interlocking structure resistant to fragmentation and is typical of many multicyclic caged hydrocarbons.²⁵ The infrared spectrum is remarkably featureless, consistent with a rigid structure of high symmetry. Apart from the CH and CH_2 bond stretching absorptions centered at 2900 cm^{-1} , there are only six sharp absorptions of moderately weak intensity. The 90-MHz ^1H -NMR spectrum of *anti*-tetramantane consists of six separate absorptions at τ 8.78 (4 H), 8.71 (4 H), 8.61 (4 H), 8.45 (4 H), 8.32 (12 H), and 8.14 (2 H). The spectrum is very similar to that of triamantane³ and comparison of the two leads to the assignments shown in Figure 1. Some features of the x-ray structure²³ of *anti*-tetramantane are shown in Table I. Classification of the C–C bond lengths according to the degree of substitution reveals a significant trend. The closer one comes to the situation in diamond itself, i.e., bonding between quaternary carbon atoms, the larger the measured bond length. Classification of the valency angles in a similar fashion shows that the largest (111.8°) and the smallest (107.4°) angles both occur at the unique quaternary carbon atom. Both result from the steric interaction between the four hydrogen atoms on next-nearest neighbors.

Experimental Section

Melting points were determined for samples sealed in capillary tubes. Unless otherwise stated IR spectral data relate to dispersions in potassium bromide disks. ^1H NMR data were measured at 60 MHz on a Varian A-60D spectrometer or at 90 MHz on a Bruker WH-90

Table I

Bond Lengths Classified According to Degree of Substitution	
	Average, Å
CH-CH	1.524
C-CH	1.528
CH-CH	1.537
C-CH	1.542

Valency Angles Classified According to Degree of Substitution of the Three Carbon Atoms	
	Average, deg
CH-C-CH	107.4
CH-C-CH ₂	109.4
CH ₂ -C-CH ₂	111.8
C-CH-CH	109.6
CH-CH-CH (eq)	108.2
(axial)	111.4
CH-CH-CH ₂	110.6
CH ₂ -CH-CH ₂	109.4
C-CH ₂ -CH	110.0
CH-CH ₂ -CH	109.4

spectrometer using tetramethylsilane as internal standard. Mass spectrometric data were obtained with an AEI MS-902 instrument at an ionizing beam energy of 70 eV. Differential thermal analysis was performed on a Du Pont 900 thermal analyzer fitted with a DSC cell. GLC refers to analysis on either 2-m Silicone Gum Rubber on Chromosorb W (2% w/w) (column A) or 2-m Silicone Nitrile Fluid XF 1150 on Chromosorb G (5% w/w) (column B). Spence type H alumina and Whatman SG 31 silica gel were used for absorption chromatography. Light petroleum had bp 40–60 °C. The drying agent employed was magnesium sulfate.

Diamantane,⁹ 1-bromodiamantane,⁹ diamantan-1-ol,⁹ and diamantane-1-carboxylic acid¹⁵ were prepared by literature procedures.

Diamantane-1-carboxylic Acid Chloride (9). To a solution of the acid (30.6 g) in dry benzene (500 mL) was added oxaloyl chloride (60 mL) and the solution was stirred at room temperature for 12 h. The solvent and excess oxaloyl chloride were removed at reduced pressure, leaving the acid chloride as a colorless, crystalline solid (29.5 g, 89%), ν_{\max} (Nujol) 1790 cm^{-1} , which was used without purification.

Diamantane-1-diazomethyl Ketone (10). A solution of the acid chloride 9 (34.9 g) in ether (500 mL) was added dropwise with stirring over 30 min to an ice-cold solution of diazomethane (prepared from 132 g of *p*-toluenesulfonylmethyl nitrosamide) in ether (860 mL). The mixture was allowed to come to room temperature and after 12 h was concentrated at reduced pressure, yielding a yellow solid. The product was triturated with cold ether (45 mL) and filtered, yielding the diazomethyl ketone (25 g, 71%) which was used without further purification.

Cyclopentanone (11). A solution of the diazomethyl ketone (10, 12.6 g) in dry toluene (500 mL) was added dropwise over 3 h to a stirred suspension of anhydrous copper sulfate (2.5 g) in boiling toluene (1.5 L). The mixture was heated under reflux for a further 3 h, then was cooled and filtered. The filtrate was washed successively with water (200 mL), 5 N NaOH (4 × 150 mL), and water (3 × 150 mL), then dried. Removal of the solvent gave an oil (11.2 g) shown by GLC analysis on column A at 220 °C to contain four components in the ratio ca. 25:5:2:1. The product was chromatographed on alumina (700 g), elution with light petroleum–ether (6:1) giving the three minor components (3.1 g), followed by the crystalline cyclopentanone (11, 5.3 g, 47%); mp 214–216 °C after sublimation; τ (CDCl_3) 7.4–8.9 (18 H) and 7.8 (2 H, doublet superimposed on main absorption); ν_{\max} 1737 cm^{-1} ; m/e (rel intensity) 228 (86, M^+), 200 (100), 143 (26), 106 (20), 105 (18), 95 (16), 94 (15), 93 (16), 92 (13), 91 (35), 79 (22), and 77 (17). Anal. ($\text{C}_{16}\text{H}_{20}\text{O}$) C, H.

Reaction of Ketone 11 with Ethylmagnesium Bromide. To an ethereal solution of ethylmagnesium bromide (prepared from 14.4 g of ethyl bromide and 3.2 g of magnesium in 150 mL of ether) was added

90 MHz ^1H -n.m.r. spectrum

Anti-tetramantane

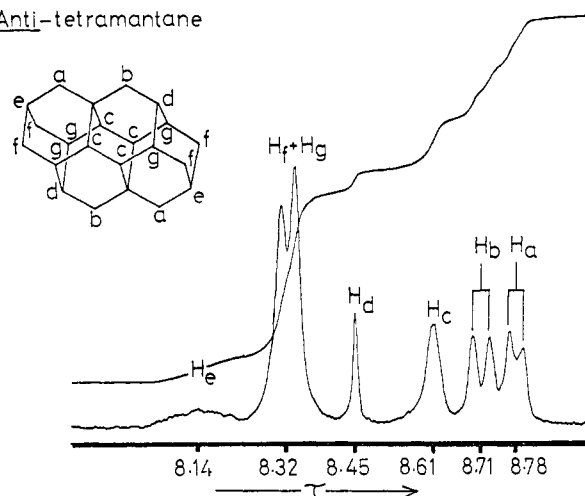


Figure 1.

an ethereal solution (100 mL) of ketone 11 (3.0 g) with stirring over 30 min. The mixture was heated under reflux for 36 h and, after cooling, saturated aqueous ammonium chloride was added. The ether layer and ether extracts of the aqueous layer (3 × 100 mL) were combined, washed with water, and dried. Removal of the solvent left a solid (3.4 g), GLC analysis of which on column B at 205 °C revealed the presence of two components, ratio 3:1, presumed to be the epimeric alcohols 12. The mixture was purified by chromatography over silica gel which afforded the isomers in 87% yield. Both isomers decomposed on heating and the following data relate to a 3:1 mixture of the two: τ (CDCl_3) 7.7–8.8 (23 H) and 9.03 (triplet, 3 H); ν_{\max} 3400 cm^{-1} ; m/e (rel intensity) 258 (15, M^+), 240 (20), 229 (100), 201 (52), 198 (75), 117 (15), 106 (12), 105 (20), 93 (17), 91 (45), 79 (25), 77 (20), 58 (37), and 57 (21).

Dehydration of Alcohols 12. A solution of the alcohols (4.1 g) in dry benzene (500 mL) containing iodine (0.05 g) was heated under reflux for 48 h with continuous removal of water. The solvent was then removed at reduced pressure and the residue was taken up in light petroleum and passed through a column of alumina (300 g). Elution with light petroleum gave the olefin 13 (3.0 g, 79%) as a crystalline solid: mp 40–41 °C after vacuum sublimation; τ (CDCl_3) 7.6–9.0 (23 H) and 5.0 (multiplet, 1 H); ν_{\max} 1680 cm^{-1} ; m/e (rel intensity) 240 (100, M^+), 225 (8), 211 (10), 156 (5), 154 (6), 146 (6), 129 (5), 117 (5), 105 (5), 93 (4), 79 (5), and 77 (6). Anal. ($\text{C}_{18}\text{H}_{24}$) C, H.

Preparation of 1.5% w/w Platinum on Silica. Silica gel (75 g) was added to chloroplatinic acid (40 mL, 5% aqueous solution) in water (150 mL) and the mixture was thoroughly shaken. Water was then removed at reduced pressure leaving the yellow platinum(IV) chloride on silica gel. Portions (ca. 5 g) of the solid were packed in a Pyrex tube and reduced in a stream of hydrogen at 450 °C for 8 h. The resulting material was approximately 1.5% w/w in platinum metal.

Rearrangement of 13 into Triamantane (3). A sample of 13 (1.144 g) was vaporized in a stream of hydrogen and passed through the catalyst bed (ca. 10 g) contained in a horizontal Pyrex tube held at 430 °C. Products were condensed from the effluent gas stream in a cold trap at –78 °C, yielding 0.766 g. GLC analysis on column A at 180 °C showed the presence of one major component and several minor components. Crystallization of the mixture from acetone gave triamantane (0.240 g, 21%), mp 224 °C (lit.³ mp 221.0–221.5 °C) with a premelting transition at 155 °C. The spectral data agreed closely with published values.³

Diamantane 1,6-Dibromide. The dibromide was obtained in 44% yield by direct bromination of diamantane as described previously²¹ and purified by recrystallization from chloroform.

Diamantane-1,6-diol. A mixture of diamantane 1,6-dibromide (85 g) and dimethylformamide (860 mL) containing 0.67 N hydrochloric acid (1050 mL) was heated under reflux with stirring for 48 h. The cooled mixture was diluted with water (1 L) and filtered. The solid was air dried and then was taken up in chloroform (1.5 L). The chloroform solution was washed with water, dried, and concentrated, yielding the diol (46.9 g, 87%) as a colorless solid. Vacuum sublimation

gave an analytically pure sample: mp 300 °C with a premelting transition at 240 °C; τ (CDCl₃) 7.7–8.9 (complex); ν_{\max} 3390 cm⁻¹; m/e (rel intensity) 220 (54, M⁺), 203 (24), 202 (100), 184 (20), 145 (14), 143 (12), 142 (15), 132 (19), 131 (68), 130 (31), 111 (23), 105 (11), 95 (30), 93 (29), 92 (25), 91 (39), 79 (25), 77 (30), 67 (20), 55 (13), and 53 (13). Anal. (C₁₄H₂₀O₂) C, H.

Diamantane-1,6-dicarboxylic Acid (14). A solution of diamantane-1,6-diol (45.9 g) in 98% formic acid (350 mL) (heating necessary) was added dropwise with stirring to 98% sulfuric acid (700 mL) at 0 °C over 3 h. After the addition the mixture was stirred at room temperature for 5 h, then was poured onto ice (1 kg). The precipitate was removed by filtration and dissolved in 5 N aqueous sodium hydroxide. The resulting solution was washed with chloroform (3 × 500 mL) and then acidified with 10 N hydrochloric acid. The diacid was obtained by filtration, washed with water, and air dried to constant weight, 57.3 g, 99.6%. An analytically pure sample was obtained by refluxing a portion in glacial acetic acid for 24 h. After cooling, the solution was poured into water and filtered. The precipitate was washed with water and then ether and dried: mp 429 °C (by differential scanning calorimetry); ν_{\max} 3400–2400 (broad) and 1685 cm⁻¹; τ (CD₃SOCD₃) 7.9–8.5 (multiplet, 14 H) and 7.91 (singlet, 4 H); m/e (rel intensity) 276 (8, M⁺), 232 (16), 231 (100), 202 (12), 185 (36), 129 (10), 105 (8), 93 (12), 92 (5), 91 (18), 79 (10), 77 (10), 67 (5), 65 (7), 55 (5), 53 (5). Anal. (C₁₆H₂₀O₄) C, H.

Diamantane-1,6-dicarboxylic Acid Chloride (15). A solution of the diacid **14** (54.7 g) in benzene (1 L) containing oxaloyl chloride (250 mL) was heated under reflux under nitrogen for 13 h. The solvent and excess oxaloyl chloride were removed at reduced pressure, yielding the bis acid chloride as a colorless solid (60.4 g, 97.7%), ν_{\max} (Nujol) 1790 cm⁻¹, which was used without purification.

Diamantane-1,6-bis(diazomethyl) Ketone (16). The reaction was conducted in five batches; a solution of the acid chloride **15** (12 g) in dry benzene (500 mL) was added dropwise with stirring to a solution of diazomethane (prepared from 107 g of *p*-toluenesulfonylmethyl-nitrosamide) in ether at 0 °C over 30 min. The mixture was allowed to stand at room temperature for 12 h and then was concentrated at reduced pressure, yielding a pale yellow solid. The product was triturated with ether, then filtered. The five batches produced a total of 48.89 g, 79.7% of the bisdiazomethyl ketone (**16**). The product was thermally unstable and was not purified further.

Diketone 17 and/or 18. Bisdiazomethyl ketone (**16**, 12.7 g) was added in small portions over 3 h to a stirred suspension of anhydrous copper sulfate (5.4 g) in boiling toluene (2 L). The mixture was heated under reflux for a further 4 h, then was cooled and filtered. The filtrate was washed successively with water (500 mL), 5 N aqueous sodium hydroxide (4 × 150 mL), and water (3 × 150 mL), and then was concentrated, yielding a brown solid (11.4 g). Calculated analysis on column A at 225 °C revealed the presence of several products. The product was chromatographed over silica gel (750 g). Elution with light petroleum–ether (1:3) gave a mixture of several components (7.1 g). Elution with ether–acetone (19:1) gave the diketone **17** and/or **18** as a colorless solid (1.6 g, 15.2%); ν_{\max} 1732 cm⁻¹; τ (CDCl₃) 7.4–8.9 (multiplet, 16 H) and 7.7 (doublet superimposed on the multiplet, 4 H); m/e (rel intensity) 268 (100, M⁺), 241 (20), 240 (90), 212 (22), 198 (19), 143 (21), 129 (25), 106 (30), 105 (29), 93 (23), 92 (19), 91 (60), 79 (28), and 77 (30). Anal. (C₁₈H₁₀O₂) C, H.

Reaction of Diketone 17 and/or 18 with Ethylmagnesium Bromide. To an ethereal solution of ethylmagnesium bromide (prepared from 15.7 g of ethyl bromide and 3.5 g of magnesium in 150 mL of ether) was added an ethereal solution (100 mL) of the diketone (1.0 g) with stirring over 30 min. The mixture was heated under reflux for 80 h and, after cooling, saturated aqueous ammonium chloride was added. The ether layer and ether extracts of the aqueous layer (3 × 100 mL) were combined, washed with water, and dried. Removal of the solvent left a colorless solid (0.98 g) which was placed on a column of silica gel (100 g). Elution with light petroleum–ether (1:1) gave the alcohols **19** and **20** (0.87 g, 69%) as a crystalline solid which decomposed on heating: ν_{\max} 3440 cm⁻¹; τ (CDCl₃) 7.7–8.9 (multiplet, 26 H) and 9.01 (triplet, 6 H); m/e (rel intensity) 328 (10, M⁺), 310 (59), 292 (100), 281 (50), 282 (50), 253 (51), 239 (70), 145 (70), 129 (45), 131 (35), 117 (50), 105 (60), 91 (90), 79 (30), 67 (20), 57 (50), 53 (20).

Dehydration of 19 and/or 20. A solution of the alcohols (0.5 g) in dry benzene (300 mL) containing iodine (0.03 g) was heated under reflux for 48 h with continuous removal of water. The solvent was removed at reduced pressure and the residue was chromatographed over alumina. Elution with light petroleum gave the diene **21** and/or

22 as a colorless solid (0.24 g, 66%); mp 142–143 °C after vacuum sublimation; τ (CDCl₃) 7.6–9.0 (multiplet, 26 H) and 5.0 (multiplet, 2 H); ν_{\max} 1685 cm⁻¹; m/e (rel intensity) 292 (100, M⁺), 145 (26), 147 (14), 144 (13), 143 (13), 142 (10), 129 (10), 131 (5), 107 (5), 105 (8), 93 (5), 91 (14), 79 (5), 77 (7), and 67 (3). Anal. (C₂₂H₂₈) C, H.

anti-Tetramantane (5). A sample of the diene **21** and/or **22** (0.30 g) was vaporized in a stream of hydrogen and passed through a horizontal bed of 1.5% platinum on silica in a Pyrex tube held at 350 °C. Products were condensed from the effluent gas stream in a cold trap at -78 °C, yielding 0.17 g. GLC analysis on column A at 200 °C revealed the absence of diene and the presence of a single long retention component and several short retention time components. Three crystallizations of the mixture from acetone gave *anti*-tetramantane (**5**) as a colorless, highly crystalline solid (0.03 g, 10%); mp 173.5–174.0 °C with a premelting transition at 159 °C; ν_{\max} 2900, 1445, 1342, 1323, 1295, 1080, and 1054 cm⁻¹; τ (CDCl₃) 8.78 (doublet, 4 H, $J = 2.5 \pm 0.2$ Hz), 8.71 (doublet, 4 H, $J = 2.9 \pm 0.2$ Hz), 8.61 (broad singlet, 4 H), 8.45 (singlet, 2 H), 8.32 (doublet, 12 H), and 8.14 (broad multiplet, 2 H); m/e (rel intensity) 292 (100, M⁺) 291 (30), 155 (5), 146 (5), 143 (5), 141 (6), 129 (6), 128 (5), 117 (5), 115 (4), 105 (7), 93 (4), 91 (13), 79 (6), 77 (5), 67 (5), and 55 (5).

Acknowledgments. We thank the Northern Ireland Department of Education for a Postgraduate Award to W.B. We are indebted to Professor G. Ferguson and Dr. P. Roberts, Department of Chemistry, University of Guelph, for the x-ray structure of *anti*-tetramantane.

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Intrinsic Asymmetry and Diastereotopism

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Abstract: The term "intrinsic asymmetry", as applied to the time-averaged anisochrony of geminal groups in systems of the type $[R^*]CU_2V$ (where R^* is a chiral perturbing group), is critically discussed against the background of symmetry criteria for chemical shift nonequivalence. It is concluded that continued use of the term is no longer justified. The symmetry requirements for time-averaged anisochrony under conditions of equipopulation of conformers are extended to the general case of an *n*-fold barrier to internal rotation. Chemical shift nonequivalence of geminal methyl groups in a compound of the type $XYZC-C\equiv C-CH(CH_3)_2$ is demonstrated and the adequacy of the free rotation (windmilling) model for such a system is discussed. It is noted that for NMR purposes, the distinction between groups diastereotopic by internal and external comparison is more a matter of convenience than of principle.

The structural criteria for magnetic shielding (or chemical shift) equivalence (isochrony) and nonequivalence (anisochrony) of nuclei have previously been discussed in terms of the symmetry relationships between molecular subunits.² Against the backdrop of this analysis, the present paper addresses the theme of "intrinsic asymmetry", which continues to be the subject of lively interest even though it has been under debate for 20 years.

Symmetry Criteria for Anisochrony

The symmetry equivalence of two or more nuclei is a sufficient but not a necessary condition for isochrony; conversely, the symmetry nonequivalence of such nuclei is a necessary but not a sufficient condition for anisochrony.³ We consider two or more nuclei symmetry equivalent if they are permutable under an operation of the appropriate molecular symmetry (MS) group.⁴ This group consists not only of the set of permutations and permutation-inversions which are feasible under the conditions of measurement, i.e., which occur on the time scale of the NMR experiment, but also of the products of these operations with rotatory reflections, since we are here concerned with measurements in achiral media. For a rigid molecule this reduces to an MS group which is isomorphic to the molecular point group.⁵ It follows that symmetry nonequivalent nuclei are not permutable under the operations of the appropriate group.

Thus expressed, the symmetry criteria for isochrony and anisochrony are independent of bonding connectivity (constitution). The pairwise bonding connectedness of atoms, as conventionally expressed by an adjacency matrix or, more commonly, by a constitutional graph, while admittedly a powerful and often indispensable symbolic tool, is fundamentally irrelevant to the question of chemical shift equivalence or nonequivalence, except insofar as it bears upon the magnitude of the effect.

For our purposes the most important consequence of this analysis is that the anisochronies of diastereotopic and constitutionally heterotopic⁶ groups stem from a single source: symmetry nonequivalence of nuclei. Stated otherwise, it is

impossible to distinguish between diastereotopic and constitutionally heterotopic nuclei solely on the basis of the observation that the nuclei are anisochronous, i.e., in the absence of ancillary information.

Accordingly, the differences in screening constants between diastereotopic groups (e.g., the geminal fluorines in $ClBrFCCF_2Br$) are dealt with by precisely the same theory as those between constitutionally heterotopic groups (e.g., the vicinal fluorines in the same molecule).⁷ Specifically, the total Hamiltonian of an isolated molecule and the associated wave functions reflect the symmetry properties of this molecule. If two nuclei are homotopic (or enantiotopic) for symmetry reasons, the electronic distributions around these nuclei are identical up to reflection. On the other hand, if two nuclei are constitutionally heterotopic or diastereotopic, they are characterized by different electronic distributions.

The symmetry properties of a molecule can of course be modified by an external perturbation, such as interaction with other molecules or with external electric or magnetic fields. The well-known transformation of isochronous enantiotopic nuclei into anisochronous nuclei by interaction with chiral solvent molecules or shift reagents exemplifies the first kind of perturbation. The modification of the symmetry properties of a molecule by a crystal lattice as observed in an external magnetic field, obviously very important in an NMR experiment, is illustrated by the work of Pausak et al.⁹ on the high-resolution ^{13}C NMR spectra of single-crystal durene (1,2,4,5-tetramethylbenzene), in which distinct signals were observed for the CH_3 groups, the chemical shift difference between these signals being a function of the orientation of the crystal with respect to the magnetic field.¹⁰

Although the screening tensor components¹⁰ are in principle accessible by quantum mechanical calculations,^{11,12} no molecules of the type $[R^*]CU_2V$ (where R^* is a chiral grouping and U is an NMR-active nucleus) have yet been studied by these methods. However, screening tensor components of diastereotopic and constitutionally heterotopic nuclei have been calculated for 1,1-difluoro-, *cis*-1,2-difluoro-, and *trans*-1,2-difluoroethylene,¹² and are in reasonable agreement with